Appl. No. 09/367,794 Amdt. dated August 6, 2003 Reply to Office Action of March 6, 2003

Please amend claims 44, 46, 48, 52, 53, 55, 59, 62, and 64 as follows:

Please cancel claims 45, 47, 51, 54, 58, and 63 without prejudice or disclaimer.

Please add new claims 67-69 as follows:

## **Listing of Claims:**

1	1-43. (Canceled)
2	44. (Currently Amended) A method for identifying targeting a drug that
3	binds at a preselected target site on a biological molecule to a specific selected protein,
4	wherein the specific selected protein is a member of a homologous protein series selected from
5	the group consisting of an ion channel and a membrane receptor, said method comprising:
6	providing said preselected target site on a biological target molecule, said
7	preselected target site having a chemically reactive group:
8	contacting said biological target molecule with a drug linked to an anchoring
9	moiety specific for said chemically reactive group; and
0	identifying said drug linked to said anchoring moiety.
1	contacting said specific selected protein with a compound having the formula
2	<u>A-L-D</u>
3	wherein:
4	A is an anchoring moiety that binds selectively, either covalently or
5	electrostatically, to a first binding site on said specific selected protein;
6	L is a linking group; and
7	D is a compound or drug that binds to a second binding site on said specific
8	selected protein, wherein said first binding site and said second binding site are distinct.
l	45. (Canceled)
i	46. (Currently Amended) The method in accordance with claim 44, wherein
2	said drug is a member of the group of small organic molecules consisting of a peptide, a
3	peptoid, a random bio-oligomer, a benzodiazepine, a hydantoin, a dipentide, a vinylogous

4	<del>polypeptide, a nonpeptidal peptidomimetic, an oligocarbamate, a peptidyl phosphonate, a</del>
5	nucleic acid, an antibody, an isoprenoid, a thiazolidinone, a metathiazanone, a pyrrolidine, a
6	morpholino compound, a cyclopentane carboxylic acid, phenyalkylamines, dihydropyridines, ar
7	antineoplastic agent and a local anesthetic.
1	47. (Canceled)
1	48. (Currently Amended) The method in accordance with claim 44, wherein
2	said specific selected protein is a member selected from the group consisting of a β-adrenergic
3	receptor, a calcium channel, a sodium channel, a potassium channel, a membrane transporter[s]
4	and a membrane receptor[s].
1	49. (Original) The method in accordance with claim 44, wherein said
2	anchoring moiety is a member selected from the group consisting of a sulfhydryl-reactive group
3	an alkylating agent and an acylating agent.
1	50. (Original) The method in accordance with claim 49, wherein said
2	anchoring moiety is a member selected from the group consisting of a methanethiosulfonyl
3	group, a dithiopyridyl group, a reactive disulfide, an $\alpha$ -halo ketone, an $\alpha$ -diazo ketone, an
4	activated ester, a pentafluorophenyl ester, and an anhydride.
1	51. (Canceled)
1	52. (Currently Amended) A method for identifying a compound of formula:
2	A-L-D
3	drug that binds at a preselected target site on a biological molecule a specific
4	selected protein, and wherein the specific selected protein is a member of a homologous protein
5	series selected from the group consisting of an ion channel and a membrane receptor, said
6	method comprising:

7	(a) providing a biological target molecule specific selected protein that
8	comprises a ehemically reactive group first binding site and a second binding site on said
9	specific selected protein;
10	(b) reacting contacting said biological target molecule specific selected
11	protein, with a compound, said compound comprising (1) A, wherein A is an anchoring moi

- and (2) L, wherein L is a linking group, wherein said anchoring moiety reacts with said chemically reactive group of said target molecule to form a covalent bond binds specifically either covalently or electrostatically as a ligand to said first binding site on said specific selected protein, thereby resulting in said anchoring moiety being attached to said target specific selected
- protein, thereby resulting in said anchoring moiety being attached to said target specific selected
- 16 <u>protein molecule through a covalent bond;</u>

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- (c) combining said target molecule specific selected protein from step (b) with one or more members of a library of drugs that are capable of covalently binding to said linking group, wherein at least one member of said library binds to a second binding site on said specific selected protein and forms a covalent bond with said linking group to form a target molecule specific selected protein conjugated to A-L-D, wherein D is at least one member of said library forming said covalent bond; and
- (d) identifying said drug, D, that forms a covalent bond with said linking group.
- 1 53. (Currently Amended) The method in accordance with claim 52, wherein
  2 said drug is a member of the group consisting of a peptide, a peptoid, a random bio-oligomer,
  3 a benzodiazepine, a hydantoin, a dipeptide, a vinylogous polypeptide, a nonpeptidal
  4 peptidomimetic, an oligocarbamate, a peptidyl phosphonate, a nucleic acid, an antibody, an
  5 isoprenoid, a thiazolidinone, a metathiazanone, a pyrrolidine, a morpholino compound, a
  6 cyclopentane carboxylic acid, phenyalkylamines, dihydropyridines, an antineoplastic agent and a
  7 local anesthetic.
  - 54. (Canceled)

1	55. (Currently Amended) The method in accordance with claim 52, wherein
2	said specific selected protein is a member selected from the group consisting of a β-adrenergic
3	receptor, a calcium channel, a sodium channel, a potassium channel, a membrane transporter[s]
4	and a membrane receptor[s].
1	56. (Original) The method in accordance with claim 52, wherein said
2	anchoring moiety is a member selected from the group consisting of a sulfhydryl-reactive group,
3	an alkylating agent and an acylating agent.
1	57. (Previously Presented) The method in accordance with claim 56, wherein
2	said anchoring moiety is a member selected from the group consisting of a methanethiosulfonyl
3	group, a dithiopyridyl group, a reactive disulfide, an $\alpha$ -halo ketone, an $\alpha$ -diazo ketone, an
4	activated ester, a pentafluorophenyl ester, and an anhydride.
1	58. (Canceled)
1	59. (Currently Amended) A method for identifying a drug that binds at a
2	preselected target site on a biological molecule to a specific selected protein, wherein the
3	specific selected protein is a member of a homologous protein series selected from the group
4	consisting of an ion channel and membrane receptor, said method comprising[:]contacting a
5	compound of formula:
6	A-L-D
7	with said specific selected protein, wherein:
8	identifying an anchoring moiety that is specific for a first target site;
9	identifying a drug that is specific for a second target site, wherein said
10	anchoring moiety and said drug are linked by a formula
11	A-L-D
12	wherein:
13	A is an anchoring moiety that binds specifically to a first target binding
14	site on said specific selected protein;

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15	L is a linking group; and
16	D is a drug that binds specifically to a second target binding site on said
17	specific selected protein, thereby identifying said drug.
1	60. (Original) The method in accordance with claim 59, wherein A is a
2	member of a combinatorial library of compounds.
1	61. (Original) The method in accordance with claim 59, wherein D is a
2	member of a combinatorial library of compounds.
-	member of a combinatorial library of compounds.
1	62. (Currently Amended) The method in accordance with claim 59, wherein
2	said drug is a member of the group of small organic molecules consisting of a peptide, a
3	peptoid, a random bio-oligomer, a benzodiazepine, a hydantoin, a dipeptide, a vinylogous
4	polypeptide, a nonpeptidal peptidomimetic, an oligocarbamate, a peptidyl phosphonate, a
5	nucleic acid, an antibody, an isoprenoid, a thiazolidinone, a metathiazanone, a pyrrolidine, a
6	morpholino compound, cyclopentane carboxylic acid, phenyalkylamines, dihydropyridines, an
7	antineoplastic agent and a local anesthetic.
1	63. (Canceled)
1	64. (Currently Amended) The method in accordance with claim 59, wherein
2	said specific selected protein is a member selected from the group consisting of a β-adrenergic
3	receptor, a calcium channel, a sodium channel, a potassium channel, a membrane transporter[s]
4	and <u>a</u> membrane receptor[s].
1	65. (Original) The method in accordance with claim 59 wherein said
2	C , who can be a second with a second state
	anchoring moiety is a member selected from the group consisting of a sulfhydryl-reactive group,
3	an alkylating agent and an acylating agent.
1	66. (Previously Presented) The method in accordance with claim 65, wherein

said anchoring moiety is a member selected from the group consisting of a methanethiosulfonyl

- group, a dithiopyridyl group, a reactive disulfide, an α-halo ketone, an α-diazo ketone, an
   activated ester, a pentafluorophenyl ester, and an anhydride.
- 1 67. (New) A method of claim 44, wherein D is a drug that binds non-2 specifically for members of a homologous protein series.
- 1 68. (New) A method of claim 44, wherein the compound of formula A-L-D is 2 selected from the group consisting of:

1	69. (New) A method for targeting a drug to a calcium ion channel protein,
2	wherein said calcium ion channel protein is located in cardiac muscle tissue, said method
3	comprising:
4	contacting said calcium ion channel protein with a compound having the formul
5	A-L-D
6	wherein:
7	A is an anchoring moiety that binds specifically to a first binding site on said
8	calcium ion channel protein;
9	L is a linking group;
10	D is a drug that binds to a second binding site on said calcium ion channel
11	protein, wherein said first binding site and said second binding site are distinct.